ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/15/2016

ClinicalTrials.gov ID: NCT00853762

Study Identification

Unique Protocol ID:	28851
Brief Title:	Atacicept in Multiple Sclerosis Extension Study, Phase II (ATAMS ext)
Official Title:	An Open-label, Multicenter Phase II Extension of Study 28063 (ATAMS) to Obtain Long-term Follow-up Data in Subjects With Relapsing Multiple Sclerosis Treated With Atacicept for up to 5 Years (ATAMS-Extension)
Secondary IDs:	

Study Status

Record Verification:	April 2016
Overall Status:	Terminated
Study Start:	March 2009
Primary Completion:	September 2009 [Actual]
Study Completion:	February 2011 [Actual]

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	Merck KGaA

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? No

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 100795 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 05Jan09 Board Name: Federal Public Service Health, Food Chain Safety and Environment Board Affiliation: Federal Agency of Medicinal and Health Products (AFMPS - FAGG), Department "Research & Development" Phone: 00 32 2 524 84 68 Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration European Union: European Medicines Agency

Study Description

Brief Summary:	This study (28851) is a long-term follow-up study of subjects enrolled in ATAMS study 28063 (NCT00642902). The aim of this study is to monitor the safety and tolerability of atacicept administered for up to 5 years to subjects with relapsing multiple sclerosis (RMS). This extension study consists of two parts. Part A will be double blind and Part B will be open label. During Part A, subjects initially randomized to atacicept will continue to receive the atacicept dose to which they have been randomized in study 28063 (ATAMS) once a week subcutaneously (under the skin). Subjects randomized to placebo in ATAMS will receive atacicept at 150 mg once a week subcutaneously during Part A. Once the results of ATAMS are available and the atacicept dose with the best benefit / risk ratio has been identified, all subjects will be switched to this dose and will continue the extension study open-label (Part B). Throughout the study, subjects and investigators will remain blinded with respect to initial and part A treatment allocation/dose.
Detailed Description:	

Conditions

Conditions:	Relapsing Multiple Sclerosis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety Study
Enrollment:	74 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Part A: Double blind: Atacicept	Drug: Atacicept Subjects who received atacicept 25 milligram (mg), 75 mg, and 150 mg subcutaneously (SC) as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg, 75 mg, and 150 mg SC for 32 weeks, in 28063 study will be continued with atacicept 25 mg, 75 mg, 150 mg and 150 mg (without loading) SC, respectively once weekly up to 5 years or up to early termination of treatment or early termination of the study. Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study will be continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Experimental: Part B: Open Label: Atacicept	Drug: Atacicept Subjects will receive the atacicept dose with best benefit/risk ratio treatment which will be identified in ATAMS study.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years

Maximum Age: 60 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Participation in study 28063.
- Completion of Week 36 visit of the core study 28063.
- Willingness and ability to comply with study procedures for the duration of the study.
- Voluntary provision of written informed consent (including, for the USA, subject authorization under the Health Insurance Portability and Accountability Act (HIPAA)), given before any study-related procedure that is not part of normal medical care and with the understanding that the subject may withdraw consent at any time without prejudice to his or her future medical care.

Exclusion Criteria:

- Premature discontinuation of core study 28063.
- Subjects who meet criteria listed below will receive IMP in study 28851:
    - Subjects who are eligible for participation in extension study 28851 but do not meet these criteria will not be treated with IMP but will undergo scheduled visits, irrespective of their treatment.
- All subjects must satisfy the following criteria before Extension Study Day 1 (D1-EXT; defined as the first day of dosing in the extension study) to be eligible for treatment with IMP:
    - Eligibility for participation in extension study 28851.
    - For women of childbearing potential, a negative urine pregnancy test at eligibility assessment.
    - Female subjects of childbearing potential must be willing to avoid pregnancy by using an adequate method of contraception for four (4) weeks before the first dose administered within the extension study, during the study and for twelve (12) weeks after the last dose of trial medication. Adequate contraception is defined as two barrier methods, or one barrier method with spermicide, or an intrauterine device, or use of a combined oral female hormonal contraceptive (or the definitions requested by health authorities and locally amended in the core study 28063). For the purposes of this trial, women of childbearing potential are defined as: "All female subjects after puberty unless they are post-menopausal for at least two years or are surgically sterile" (For Germany Only: Female subjects of childbearing potential must be willing to avoid pregnancy by using highly effective methods of contraception for approximately four (4) weeks prior to D1-EXT, during and for twelve (12) weeks after the last dose of trial medication. This requirement does not apply to surgically sterile subjects or to subjects who are postmenopausal for at least 2 years. Highly effective contraception is defined as any method or combination of methods which result in a low failure rate (i.e. less than (<) 1% per year) when used consistently and correctly, such as implants, injectables, combined oral contraceptives, sexual abstinence, vasectomized partner, 2 barrier methods, or 1 barrier method with spermicide)
- Willingness and ability to comply with study procedures for the duration of the study.
- To be eligible for treatment with investigational medicinal product (IMP) in study 28851, the subjects must not meet any of the following criteria:
- Non-eligibility for participation in extension study 28851 (premature discontinuation of core study 28063).
- Major protocol violation or non-compliance in the core study.
- Use of prohibited immunomodulatory / immunosuppressive therapies

- Serum immunoglobulin G (IgG) level <3 gram per liter (g/L) if the subject received atacicept in the core study, or serum IgG level <6 g/L if the subject received placebo in the core study (to protect the blinding of the core study, the IgG level will be communicated to the treating physician only if it is too low for extension study participation and only after all Week 36 assessments performed within the core study have been completed).
- Any condition, including laboratory findings that, in the opinion of the Investigator, constitutes a risk or a contraindication for participation in the extension study, or that could interfere with the study objectives, conduct or evaluation.
- Known active clinically significant acute or chronic infection, or any major episode of infection requiring hospitalization or treatment with parenteral anti-infectives.
- Investigator judgement that treatment of the subject with atacicept in the extension study is not appropriate.
- Aspartate aminotransferase (AST), or alanine aminotransferase (ALT), or alkaline phosphatase (AP) level greater than (>)2.5 x upper limit of normal (ULN), or total bilirubin >1.5 x ULN at eligibility assessment.
- Clinically significant abnormality in any hematological test (e.g. hemoglobin <100 g/L (6.21 millimoles per liter [mmol/L]), white blood cells <3 x 10^9 per liter (/L), platelets <100 x 10^9/L) at eligibility assessment.
- Clinically significant abnormality on electrocardiogram (ECG) performed at eligibility assessment.
- Presence of uncontrolled or New York Health Association (NYHA) class 3 or 4 congestive heart failure at Week 36 of the core study.
- Moderate to severe renal impairment (creatinine clearance <50 milliliter per minute (mL/min) according to Cockcroft-Gault equation).
- Allergy or hypersensitivity to gadolinium (Gd).
- Allergy or hypersensitivity to atacicept or to any of the components of the formulated atacicept.
- Diagnosis or family history of Creutzfeldt-Jakob disease (CJD).

Contacts/Locations

Study Officials: Daniel Mikol, MD, PhD
Study Director
EMD Serono

Locations: United States, Arizona
Research Site
Phoenix, Arizona, United States

United States, Michigan
Research Site
East Lansing, Michigan, United States

United States, Ohio
Research Site
Cleveland, Ohio, United States

Research Site
Cleveland,, Ohio, United States

United States, Tennessee

Research Site
Nashville, Tennessee, United States

United States, Pennsylvania
Research Site
Philadelphia, Pennsylvania, United States

United States, Illinois
Research Site
Northbrook, Illinois, United States

Canada, Ontario
Research Site
Ottawa, Ontario, Canada

Canada, Alberta
Research Site
Calgary, Alberta, Canada

Switzerland
Research Site
Basel, Switzerland

Research Site
Zürich, Switzerland

Research Site
Innsbruck, Switzerland

Belgium
Research Site
Diepenbeek, Belgium

Research Site
Sijsele, Belgium

Lithuania
Research Site
Kaunas, Lithuania

Spain
Research Site
Malaga, Spain

Czech Republic
Research Site

Brno, Czech Republic

Research Site
Hradec Králové, Czech Republic

Spain
Research Site
Madrid, Spain

Research Site
Barcelona, Spain

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London, United Kingdom

Research Site
Sheffield, United Kingdom

Research Site
Stoke on Trent, United Kingdom

France
Research Site
Saint-Herblain, France

Research Site
Caen, France

Netherlands
Research Site
Nieuwegein, Netherlands

Research Site
Rotterdam, Netherlands

Research Site
Breda, Netherlands

Sweden
Research Site
Stockholm, Sweden

Germany
Research Site
Düsseldorf, Germany

Research Site
Bochum, Germany

Australia
Research Site
Box Hill VIC, Australia

Research Site
Woodville, Australia

Research Site
New Lambton, Australia

Research Site
Fitzroy, Australia

Lebanon
Research Site
Beyrouth, Lebanon

Russian Federation
Research Site
Moscow, Russian Federation

Research Site
Vladimir, Russian Federation

Research Site
Saint Petersburg, Russian Federation

Research Site
Samara, Russian Federation

Research Site
Yaroslavl, Russian Federation

Research Site
Ekaterinburg, Russian Federation

Ukraine
Research Site
Kyiv, Ukraine

Research Site
Odessa, Ukraine

Research Site
Uzhgorod, Ukraine

Research Site
Kharkiv, Ukraine

Russian Federation
Research Site
Novosibirsk, Russian Federation

New Caledonia
Research Site
Winston Salem, New Caledonia

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First/last participant (informed consent): 03 March 2009/13 August 2009. Last participant completed: 09 September 2009.
Pre-Assignment Details	A total of 324 subjects were screened and 255 were enrolled in ATAMS (28063; NCT00642902). Overall, 75 subjects randomized and treated in ATAMS were eligible to enter ATAMS Extension. However, 74 subjects were included in ATAMS Extension and 1 subject could not enter due to the premature termination of the trial.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 milligram (mg) subcutaneously (SC) as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Overall Study

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Started	16	19	17	22
Completed	0	0	0	0
Not Completed	16	19	17	22
Premature Termination	16	15	14	21
Protocol Violation	0	0	0	1
Withdrawal by Subject	0	0	1	0
Unspecified	0	2	0	0
Randomised but not Treated	0	2	2	0

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population included all randomized subjects.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Baseline Measures

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)	Total
Number of Participants	16	19	17	22	74
Age, Continuous [units: years] Mean (Standard Deviation)	39.4 (8.4)	36.8 (9.1)	37.4 (11.2)	34.4 (8.6)	36.8 (9.3)
Gender, Male/Female [units: participants]					
Female	8	12	8	16	44
Male	8	7	9	6	30

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Injection Site Reactions, Infections, and Malignancies by Severity
Measure Description	TEAEs were defined as AEs with a start date after or on the date of the first DB treatment injection in ATAMS Extension and that occurred anytime after treatment discontinuation, or up to the day before first Rebif® rescue medication injection in ATAMS Extension. A serious TEAE was an AE that resulted in any of the following: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAE severity was graded as per Qualitative Toxicity Scale. Local injection site reactions (injection site: pain, redness, itching and swelling) throughout ATAMS Extension, starting after the first trial medication administration. If the subject experienced 1 or more of the above injection site symptoms, these were reported with the AE verbatim term “injection site reaction”. For all randomized subjects, there was an option of rescue treatment with Rebif® for 1 year beginning with the first injection of Rebif®).

Time Frame	From the first dose of study drug administration up to Week 24
Safety Issue?	Yes

Analysis Population Description

Double-blind safety analysis set included all the subjects who received at least 1 dose of trial medication in the ATAMS extension study.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	17	15	22
Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Injection Site Reactions, Infections, and Malignancies by Severity [units: Subjects]				
Mild TEAEs	5	8	8	13
Moderate TEAEs	2	4	6	4
Severe TEAEs	0	0	0	1
Mild serious TEAEs	0	0	0	0
Moderate serious TEAEs	0	1	0	0
Severe serious TEAEs	0	0	0	0

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Mild injection site reaction	2	2	5	5
Moderate injection site reaction	0	0	0	2
Severe injection site reaction	0	0	0	0
Mild infections	1	2	4	6
Moderate infections	0	1	2	0
Severe infections	0	0	0	0
Mild malignancies	0	0	0	0
Moderate malignancies	1	0	0	0
Severe malignancies	0	0	0	0

2. Primary Outcome Measure:

Measure Title	Change From Baseline in Vital Signs: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)
Measure Description	Blood pressure (systolic and diastolic) was measured after at least 3 minutes resting, with the subject in the seated position.
Time Frame	Baseline, Week 2, 4, 8, 12, 16, 20, 24 and 36
Safety Issue?	Yes

Analysis Population Description

Double-blind safety analysis set included all the subjects who received at least 1 dose of trial medication in the ATAMS extension study. Here 'n' signifies those subjects who were evaluable for the specified category.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	17	15	22
Change From Baseline in Vital Signs: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) [units: millimeter of mercury (mmHg)] Mean (Standard Deviation)				
SBP: Week 2 (n = 13, 16, 14, 20)	2.6 (8.3)	-3.0 (9.5)	-1.2 (10.7)	-0.2 (9.8)
SBP: Week 4 (n = 15, 14, 12, 21)	2.1 (7.9)	-2.4 (13.7)	-5.1 (12.6)	-0.1 (9.9)
SBP: Week 8 (n = 13, 11, 12, 16)	0.8 (10.5)	-2.1 (12.0)	-1.1 (12.5)	0.4 (11.0)
SBP: Week 12 (n = 11, 12, 8, 16)	3.0 (11.7)	-5.8 (15.3)	-3.4 (10.2)	-0.9 (11.3)
SBP: Week 16 (n=7, 9, 6, 12)	5.9 (13.4)	-9.0 (18.6)	-2.0 (12.2)	-2.3 (10.0)
SBP: Week 20 (n=3, 7, 2, 6)	2.0 (23.1)	-9.7 (14.8)	-0.5 (0.7)	3.3 (6.0)
SBP: Week 24 (n=2, 4, 1, 6)	5.0 (7.1)	-5.0 (4.1)	10.0 (NA) [1]	-5.3 (7.7)
SBP: Week 36 (n=0, 1, 0, 0)	NA (NA) [2]	-18.0 (NA) [1]	NA (NA) [2]	NA (NA) [2]
DBP: Week 2 (n=15, 13, 14, 21)	-2.1 (8.2)	-1.9 (8.4)	-3.6 (10.6)	0.3 (8.6)
DBP: Week 4 (n=15, 14, 12, 21)	-0.5 (9.0)	-0.4 (8.7)	-5.1 (9.2)	0.1 (7.7)
DBP: Week 8 (n=13, 11, 12, 16)	-2.8 (7.7)	-1.6 (8.7)	-5.9 (10.2)	0.1 (11.0)
DBP: Week 12 (n=11, 12, 8, 16)	-3.8 (11.1)	-4.8 (8.1)	-3.5 (9.9)	-2.4 (10.3)
DBP: Week 16 (n=7, 9, 6, 12)	-1.6 (14.2)	-2.9 (9.0)	-2.3 (4.2)	-1.6 (7.7)
DBP: Week 20 (n=3, 7, 2, 6)	-2.0 (17.1)	-4.4 (6.0)	2.0 (4.2)	3.7 (6.3)
DBP: Week 24 (n=2, 4, 1, 6)	0.0 (0.0)	-6.3 (2.5)	0.0 (NA) [1]	-1.0 (9.8)

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
DBP: Week 36 (n=0, 1, 0, 0)	NA (NA) [2]	-8.0 (NA) [1]	NA (NA) [2]	NA (NA) [2]

[1] Standard deviation is not evaluable as only 1 subject was evaluated for this parameter.
[2] The number of subjects evaluated was zero. Hence, data is not available.

3. Primary Outcome Measure:

Measure Title	Change From Baseline in Vital Signs: Pulse Rate
Measure Description	
Time Frame	Baseline, Week 2, 4, 8, 12, 16, 20, 24 and 36
Safety Issue?	Yes

Analysis Population Description

Double-blind safety analysis set included all the subjects who received at least 1 dose of trial medication in the ATAMS extension study. Here 'n' signifies those subjects who were evaluable for the specified category.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	17	15	22
Change From Baseline in Vital Signs: Pulse Rate [units: beats per minute (beats/min)] Mean (Standard Deviation)				
Week 2 (n=15, 13, 14, 21)	-2.1 (5.1)	-3.5 (5.5)	-3.8 (10.4)	3.6 (11.4)
Week 4 (n=15, 14, 12, 21)	0.6 (8.7)	-0.6 (9.2)	0.7 (8.2)	2.0 (8.0)
Week 8 (n=13, 11, 12, 16)	-1.7 (9.2)	-3.4 (9.1)	1.3 (8.7)	4.4 (12.4)
Week 12 (n=11, 12, 8, 16)	-0.5 (6.2)	0.7 (9.5)	-1.5 (8.9)	4.5 (9.5)
Week 12 (n=11, 12, 8, 16)	-0.5 (6.2)	0.7 (9.5)	-1.5 (8.9)	4.5 (9.5)
Week 16 (n=7, 9, 6, 12)	3.9 (4.7)	1.1 (10.5)	-0.2 (4.8)	3.8 (9.1)
Week 20 (n=3, 7, 2, 6)	-0.3 (2.1)	3.9 (8.3)	-5.0 (9.9)	11.0 (8.8)
Week 24 (n=2, 4, 1, 6)	2.5 (0.7)	-5.3 (9.4)	-22.0 (NA) [1]	9.0 (5.3)
Week 36 (n=0, 1, 0, 0)	NA (NA) [2]	7.0 (NA) [1]	NA (NA) [2]	NA (NA) [2]

[1] Standard deviation is not applicable as only 1 subject was evaluable for this parameter
[2] The number of subjects evaluable was zero. Hence, data is not available.

4. Primary Outcome Measure:

Measure Title	Change From Baseline in Vital Signs: Temperature
Measure Description	
Time Frame	Baseline, Week 2, 4, 8, 12, 16, 20, 24 and 36
Safety Issue?	Yes

Analysis Population Description

Double-blind safety analysis set included all the subjects who received at least 1 dose of trial medication in the ATAMS extension study. Here 'n' signifies those subjects who were evaluable for the specified category.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	17	15	22
Change From Baseline in Vital Signs: Temperature [units: Degree Celsius] Mean (Standard Deviation)				
Week 2 (n=15, 13, 14, 21)	-0.09 (0.27)	0.09 (0.27)	0.03 (0.21)	-0.07 (0.36)
Week 4 (n=15, 14, 12, 21)	-0.03 (0.24)	0.05 (0.42)	0.03 (0.24)	-0.12 (0.31)
Week 8 (n=13, 11, 12, 16)	-0.03 (0.40)	0.05 (0.10)	0.03 (0.28)	-0.14 (0.25)
Week 12 (n=11, 12, 8, 16)	0.02 (0.19)	0.08 (0.36)	0.09 (0.57)	-0.15 (0.34)
Week 16 (n=7, 9, 6, 12)	-0.10 (0.21)	0.17 (0.35)	-0.05 (0.23)	0.01 (0.42)
Week 20 (n=3, 7, 2, 6)	-0.37 (0.35)	0.16 (0.56)	-0.25 (0.07)	-0.08 (0.45)
Week 24 (n=2, 4, 1, 6)	0.05 (0.07)	0.30 (0.59)	0.00 (NA) [1]	-0.07 (0.26)
Week 36 (n=0, 1, 0, 0)	NA (NA) [2]	0.70 (NA) [1]	NA (NA) [2]	NA (NA) [2]

[1] Standard deviation is not applicable as only 1 subject was evaluable for this parameter.
[2] The number of subjects evaluable was zero. Hence, data is not available.

5. Primary Outcome Measure:

Measure Title	Change From Baseline in Electrocardiogram (ECGs)
Measure Description	
Time Frame	Baseline, Week 12 and 36
Safety Issue?	Yes

Analysis Population Description

No summary tables were prepared for ECG parameters, and ECG data were not formally analyzed. However, a qualitative assessment of ECG morphology and rhythm was made by the Investigator and recorded in the electronic case report form (eCRF). ECG abnormalities considered significant by the investigator were reported as AEs.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

6. Primary Outcome Measure:

Measure Title	Number of Subjects With Worsened Post Baseline Shift in Immunoglobulin A (IgA), IgG and IgM Levels

Measure Description	Number of subjects with shifts from normal Grade (Grade 0) at Baseline to worse value at post-baseline (Grade 1 to Grade 4) according to the following criteria: IgA Grade 0: greater than or equal to (>=) lower limit normal (LLN) 0.7 gram per liter (g/L); Grade 1: less than (<) LLN - 0.5 g/L, Grade 2: <0.5g/L -0.3 g/L, Grade 3: <0.3 g/L -0.1 g/L, Grade 4: < 0.1 g/L; IgG Grade 0: >= LLN (7 g/L), Grade 1: < LLN - 5 g/L, Grade 2: <5g/L -4 g/L, Grade 3: <4 g/L -3 g/L and Grade 4: < 3 g/L; IgM Grade 0: >= LLN (0.4 g/L), Grade 1: < LLN - 0.3 g/L, Grade 2: <0.3 g/L -0.2 g/L, Grade 3: <0.2 g/L -0.1 g/L, and Grade 4: < 0.1 g/L are presented in this outcome measure.
Time Frame	Baseline up to Week 36
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population included all randomized subjects.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	19	17	22
Number of Subjects With Worsened Post Baseline Shift in Immunoglobulin A (IgA), IgG and IgM Levels [units: Subjects]				
IgA	1	3	10	9
IgG	4	8	12	5
IgM	7	6	14	7

7. Primary Outcome Measure:

Measure Title	Number of Subjects With Positive Neutralizing Antibody (NAb)
Measure Description	
Time Frame	Baseline, Week 12 and 36
Safety Issue?	No

Analysis Population Description

Appropriate method/test was not established to identify the positive neutralizing antibodies for atacicept. Hence, this outcome measure was not assessed.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

8. Secondary Outcome Measure:

Measure Title	Number of Subjects With Clinical Attacks/Relapses

Measure Description	A clinical attack/relapse was defined as the fulfillment of all the following criteria: a. Neurological abnormality, either newly appearing or re-appearing, with abnormality specified by both i) neurological abnormality separated by at least 30 days from onset of a preceding clinical event, and ii) neurological abnormality lasting for at least 24 hours. b. Absence of fever or known infection (fever with temperature (axillary, orally, or intra-auriculary) > 37.5°C/99.5 °Fahrenheit). c. Objective neurological impairment, correlating with the subject's reported symptoms, defined as either i) increase in at least 1 of the functional systems of the Expanded Disability Status Scale (EDSS), or ii) increase of the total EDSS score. EDSS overall score ranging from 0 (normal) to 10 (death due to MS) was calculated.
Time Frame	Baseline up to Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population included all randomized subjects.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	19	17	22
Number of Subjects With Clinical Attacks/Relapses [units: Subjects]				
No Relapse	16	16	15	21

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
1 Relapse	0	3	2	1
2 Relapse	0	0	0	0
3 Relapse	0	0	0	0
Greater than or equal to (>=) 4 Relapse	0	0	0	0

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Expanded Disability Status Scale (EDSS) Scores at Week 12
Measure Description	EDSS is an ordinal scale in half-point increments that qualifies disability in participants with multiple sclerosis (MS). It assesses the 8 functional systems (visual, brainstem, pyramidal, cerebellar, sensory, bowel/bladder, cerebral and other) as well as ambulation. EDSS overall score ranging from 0 (normal) to 10 (death due to MS) was calculated.
Time Frame	Baseline, Week 12
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population included all randomized subjects. "N" signifies (total number of subjects analyzed) the number of evaluable subjects for this outcome measure.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	11	13	10	16
Change From Baseline in Expanded Disability Status Scale (EDSS) Scores at Week 12 [units: Units on a scale] Mean (Standard Deviation)	0.09 (0.58)	0.04 (0.97)	0.50 (0.85)	-0.06 (0.75)

10. Secondary Outcome Measure:

Measure Title	Change in Multiple Sclerosis Functional Composite (MSFC) Score at Week 12
Measure Description	The MSFC is a multidimensional clinical outcome measure which consists of three sub-tests; Timed 25-Foot Walk, 9-Hole Peg Test and Paced Auditory Serial Addition Test-3(PASAT-3). The Timed 25-Foot Walk is a quantitative measure of lower extremity function. The 9-Hole Peg Test is a quantitative measure of upper extremity (arm and hand) function. The PASAT is a measure of cognitive function that specifically assesses auditory information processing speed and flexibility, as well as calculation ability. Standardized results (Z-scores) of these sub-tests and the overall MSFC Z-score as an average of these three Z-scores was calculated. Higher Z-scores reflect better neurological function and a positive change from baseline indicates improvement. An increase in score indicates an improvement (range -3 to +3).
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population included all randomized subjects. "N" signifies number of evaluable subjects for this outcome measure.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	11	13	9	16
Change in Multiple Sclerosis Functional Composite (MSFC) Score at Week 12 [units: z-score] Mean (Standard Deviation)	0.21 (0.40)	0.04 (0.47)	-0.01 (0.24)	0.07 (0.34)

11. Secondary Outcome Measure:

Measure Title	Magnetic Resonance Imaging (MRI) Parameters: Number of T1 Gadolinium (Gd)-Enhancing Lesions Per Subject
Measure Description	
Time Frame	Baseline, Week 12 and 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population included all randomized subjects. “n” signifies the number of evaluable subjects for this outcome measure.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	19	17	22
Magnetic Resonance Imaging (MRI) Parameters: Number of T1 Gadolinium (Gd)-Enhancing Lesions Per Subject [units: Number of lesions per subject] Mean (Standard Deviation)				
Baseline (n=16, 19, 17, 22)	1.1 (2.2)	2.3 (5.0)	0.8 (1.4)	0.9 (1.4)
Week 12 (n=11, 11, 7, 15)	0.27 (0.47)	0.64 (1.29)	1.00 (1.15)	2.27 (7.16)
Week 24 (n=2, 3, 1, 6)	0.00 (0.00)	2.00 (2.00)	0.00 (0.00)	0.83 (0.75)

12. Secondary Outcome Measure:

Measure Title	Magnetic Resonance Imaging (MRI) Parameters: Volume of T2 Lesions (New or Enlarging T2 Lesions) Per Subject
Measure Description	
Time Frame	Baseline, Week 12 and Week 24
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	16	19	17	22
Magnetic Resonance Imaging (MRI) Parameters: Volume of T2 Lesions (New or Enlarging T2 Lesions) Per Subject [units: Cubic millimeter] Mean (Standard Deviation)				
Baseline (n=16, 19, 17, 22)	4792.76 (3152.56)	8196.59 (8888.74)	6158.04 (7945.59)	5868.84 (7170.81)
Week 12 (n=11, 11, 7, 15)	5604.42 (5154.52)	7634.89 (6340.19)	4934.03 (4802.98)	5365.63 (7445.87)
Week 24 (n=2, 3, 1, 6)	1699.60 (586.76)	6814.60 (6643.00)	1931.40 (0.00)	5541.80 (5614.73)

13. Secondary Outcome Measure:

Measure Title	Concentrations of Free and Total Atacicept
Measure Description	
Time Frame	Baseline and Week 12
Safety Issue?	No

Analysis Population Description

This outcome measure was not assessed due to lack of a valid assay during the usable time period of the samples.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

14. Secondary Outcome Measure:

Measure Title	Free B-Lymphocyte Stimulator (BLyS) and Free A Proliferation-Inducing Ligand (APRIL) Serum Concentrations.
Measure Description	Levels of free APRIL and free BLyS: Free APRIL serum samples were to be analyzed by using a validated enzyme-linked immunosorbent assay (ELISA) with limits of detection of 0.3125 nanogram per milliliter (ng/mL) for free APRIL and free BlyS serum samples were analysed using a validated ELISA with limits of detection of 1.56 ng/mL.
Time Frame	Baseline, Week 12 and 36
Safety Issue?	No

Analysis Population Description

This outcome measure was not assessed due to lack of a valid assay for measuring BLyS and APRIL.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

15. Secondary Outcome Measure:

Measure Title	Pharmacogenetics/Pharmacogenomics Analysis
Measure Description	Gene expression profiling and gene polymorphism identification were to be used to identify putative markers for response to treatment. • Genome-wide gene polymorphism characterization by genome-wide scan. • Targeted gene polymorphism identification of B-Lymphocyte Stimulator (BLyS) , APRIL, (receptor for B cell activating factor of the tumor necrosis factor [TNF] family) BAFF-R, (Transmembrane Activator) TACI and (B Cell Maturation Antigen) BCMA and HLA-DRB1 by direct genotyping or sequencing .
Time Frame	Day 1 and Week 36
Safety Issue?	No

Analysis Population Description

Genetic/genomic analysis was not performed as the trial was terminated early.

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Measured Values

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

Reported Adverse Events

Time Frame	From the first dose of study drug administration up to Week 24
Additional Description	[Not specified]

Reporting Groups

	Description
Atacicept 25 mg (With Loading)	Subjects who received atacicept 25 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 25 mg SC for 32 weeks, in 28063 study were continued with atacicept 25 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 75 mg (With Loading)	Subjects who received atacicept 75 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 75 mg SC for 32 weeks, in 28063 study were continued with atacicept 75 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

	Description
Atacicept 150 mg (With Loading)	Subjects who received atacicept 150 mg SC as loading dose twice weekly for first 4 weeks, followed by atacicept 150 mg SC for 32 weeks, in 28063 study were continued with atacicept 150 mg SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.
Atacicept 150 mg (Without Loading)	Subjects who received placebo SC as loading dose twice weekly for first 4 weeks, followed by placebo SC for 32 weeks, in 28063 study were continued with atacicept 150 mg (without loading dose) SC once weekly up to 5 years or up to early termination of treatment or early termination of the study.

Serious Adverse Events

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/16 (0%)	1/19 (5.26%)	0/17 (0%)	0/22 (0%)
General disorders				
Peripheral Edema [A] *	0/16 (0%)	1/19 (5.26%)	0/17 (0%)	0/22 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 11.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/16 (37.5%)	9/17 (52.94%)	8/15 (53.33%)	12/22 (54.55%)
Blood and lymphatic system disorders				
Leukocytosis [A] *	1/16 (6.25%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Leukopenia [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Lymphopenia [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Neutropenia [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Neutrophilia [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Cardiac disorders				

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cardiomyopathy [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Sinus bradycardia [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Ear and labyrinth disorders				
Vertigo positional [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Gastrointestinal disorders				
Flatulence [A] *	0/16 (0%)	1/17 (5.88%)	1/15 (6.67%)	0/22 (0%)
Teething [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
General disorders				
Fatigue [A] *	0/16 (0%)	2/17 (11.76%)	0/15 (0%)	0/22 (0%)
Injection site pruritus [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Injection site reaction [A] *	2/16 (12.5%)	2/17 (11.76%)	5/15 (33.33%)	7/22 (31.82%)
Infections and infestations				
Acute sinusitis [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Acute tonsillitis [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Ear infection [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Herpes zoster [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Influenza [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	1/22 (4.55%)
Nasopharyngitis [A] *	0/16 (0%)	1/17 (5.88%)	3/15 (20%)	2/22 (9.09%)
Respiratory tract infection viral [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Rhinitis [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Vaginitis bacterial [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Viral upper respiratory tract infection [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	1/22 (4.55%)

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Injury, poisoning and procedural complications				
Rib fracture [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Investigations				
Bilirubin urine [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Body temperature increased [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Creatinine renal clearance increased [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Electrocardiogram T wave abnormal [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Electrocardiogram repolarisation abnormality [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Gamma-glutamyltransferase increased [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Weight increased [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	1/22 (4.55%)
White blood cells urine positive [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Metabolism and nutrition disorders				
Vitamin D deficiency [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	0/16 (0%)	0/17 (0%)	2/15 (13.33%)	0/22 (0%)
Back pain [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Bursitis [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Intervertebral disc degeneration [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Myalgia [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Neck pain [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	1/22 (4.55%)
Osteoarthritis [A] *	0/16 (0%)	1/17 (5.88%)	1/15 (6.67%)	0/22 (0%)

	Atacicept 25 mg (With Loading)	Atacicept 75 mg (With Loading)	Atacicept 150 mg (With Loading)	Atacicept 150 mg (Without Loading)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Spinal column stenosis [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Uterine leiomyoma [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Nervous system disorders				
Dizziness [A] *	0/16 (0%)	1/17 (5.88%)	1/15 (6.67%)	0/22 (0%)
Dysgeusia [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	1/22 (4.55%)
Headache [A] *	0/16 (0%)	3/17 (17.65%)	1/15 (6.67%)	2/22 (9.09%)
Lumbar radiculopathy [A] *	1/16 (6.25%)	0/17 (0%)	0/15 (0%)	0/22 (0%)
Sinus headache [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Trigeminal neuralgia [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Psychiatric disorders				
Depression [A] *	0/16 (0%)	1/17 (5.88%)	1/15 (6.67%)	0/22 (0%)
Libido decreased [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Tic [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Reproductive system and breast disorders				
Erectile dysfunction [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Skin and subcutaneous tissue disorders				
Dermatitis atopic [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	0/22 (0%)
Vascular disorders				
Hot flush [A] *	0/16 (0%)	0/17 (0%)	1/15 (6.67%)	0/22 (0%)
Hypertension [A] *	0/16 (0%)	1/17 (5.88%)	0/15 (0%)	1/22 (4.55%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 11.1

Limitations and Caveats

EMD Serono voluntarily decided to terminate this trial after observing increased MS disease activity in trial 28063 ATAMS.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The study as a whole will be published prior to any individual investigator publications. It is required that copies of all papers, abstracts, articles, etc. that contain study data are to be forward to the Sponsor for review 30 days prior to submission for publication.

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